

APPENDIX A

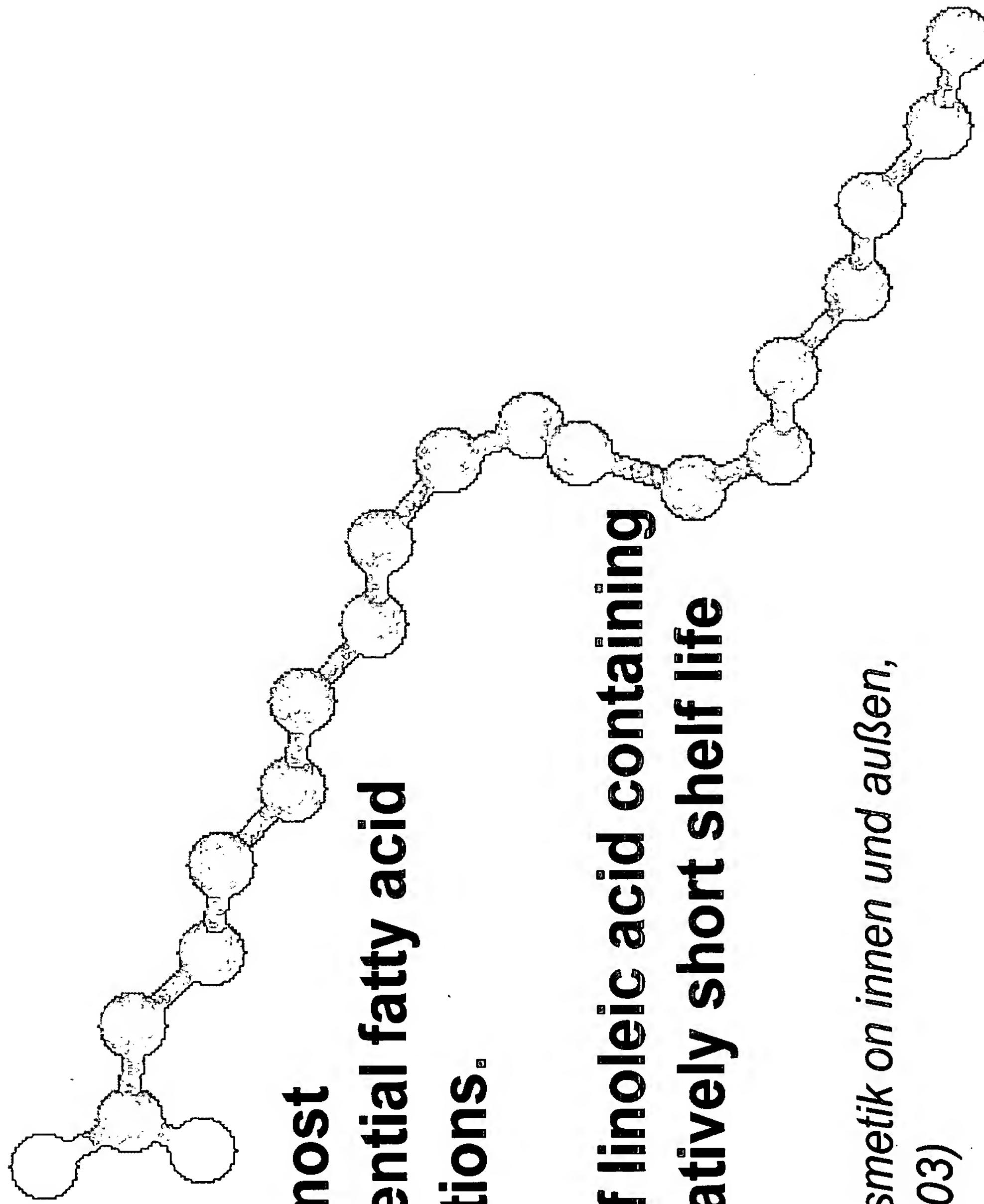
WACKER FINE CHEMICALS

CYCLODEXTRINS ANOTHER TOOL FOR
ENCAPSULATION OF LINOLEIC ACID

Regent Marlies, Kupka Michaela, Sigl Harald, F-I-P, March 2005

CREATING TOMORROW'S SOLUTIONS

LINOLEIC ACID, C₁₇H₃₁COOH,
E.G. (Z,Z)-9,12-OCTADECA DIENOIC ACID

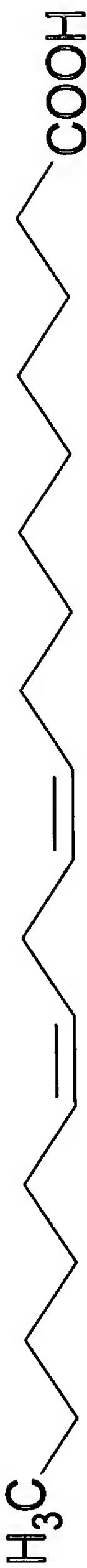


**Linoleic acid is the most
frequently used essential fatty acid
in cosmetic formulations.**

**One disadvantage of linoleic acid containing
oils is there comparatively short shelf life**

(Essentielle Fettsäuren - Kosmetik on innen und außen,
Dr. Hans Lautenschläger, 2003)

FUNCTION, PHYSIOLOGICAL EFFECTS



- Belongs to the group of omega-6 fatty acids
- It cannot be synthesized by animals
- Linoleic acid is incorporated in the skin to the most important barrier-active "ceramide" (Essentielle Fettsäuren - Kosmetik von innen und außen, Dr. Hans Lautenschläger, 2003)
- Is essential for the human body

FUNCTION, PHYSIOLOGICAL EFFECTS

- Is important for the synthesis of eicosanoids, which have a regulatory action in various tissues

(Technical Information BASF,
„products for the food and pharmaceutical industry“, 2002)

- A lack of linoleic acid in the skin has e.g. the effect of:
 - barrier disruption of the skin
 - a higher rate of the trans-epidermal water-loss
 - the skin becomes dry, scaly and gets a unhealthy colour
- Acts both as a concentrated energy carrier and as a starting material for the synthesis of arachidonic acid (important component of cell membranes)
(Technical Information BASF,
„products for the food and pharmaceutical industry“, 2002)

FUNCTION, PHYSIOLOGICAL EFFECTS

- Requirements / intake recommendations:
the adult requirement of linoleic acid is 8 – 10g per day
- There is an increased requirement for essential fatty acids after severe accidents and in certain diseases

PROPERTIES AND OCCURRENCE

- Is a colorless to straw colored liquid
- Insoluble in water, soluble in oil and fats
- Is the most common polyunsaturated fatty acid
- Linoleic acid also may convert to a isomeric unsaturated conjugated fatty-acid
- It is easily oxidized by air to peroxides that have undesirable biological effects
- Vegetable oils become rancid when exposed to air at room-temperature and can seriously spoil the taste, odor and stability of food products
- It is found in nature in plants and animal tissues

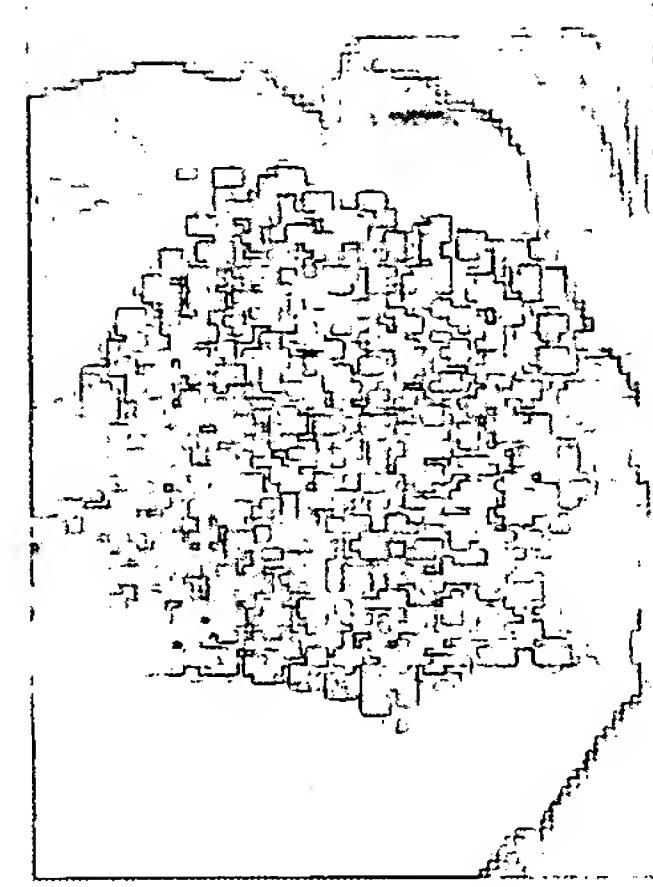
OCCURRENCE



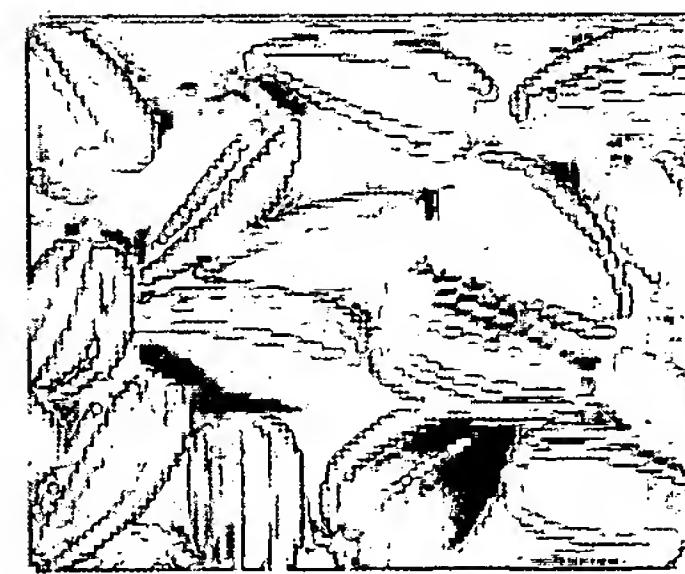
Walnut



peanut



soya



Corn

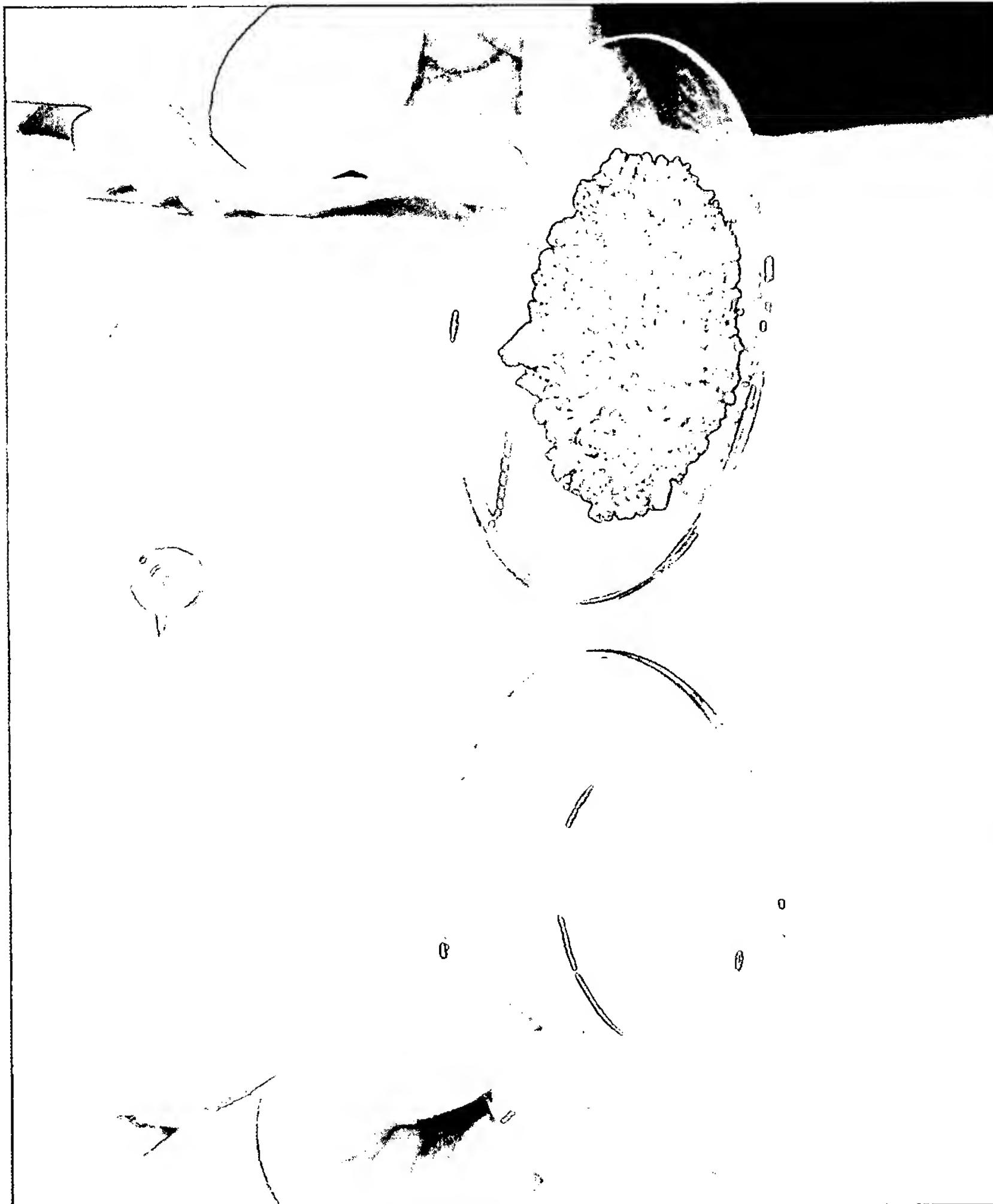
seeds of sunflower

CONVERSION FROM LIQUID TO SOLID COMPLEX

Left:
pure linoleic acid

Right:

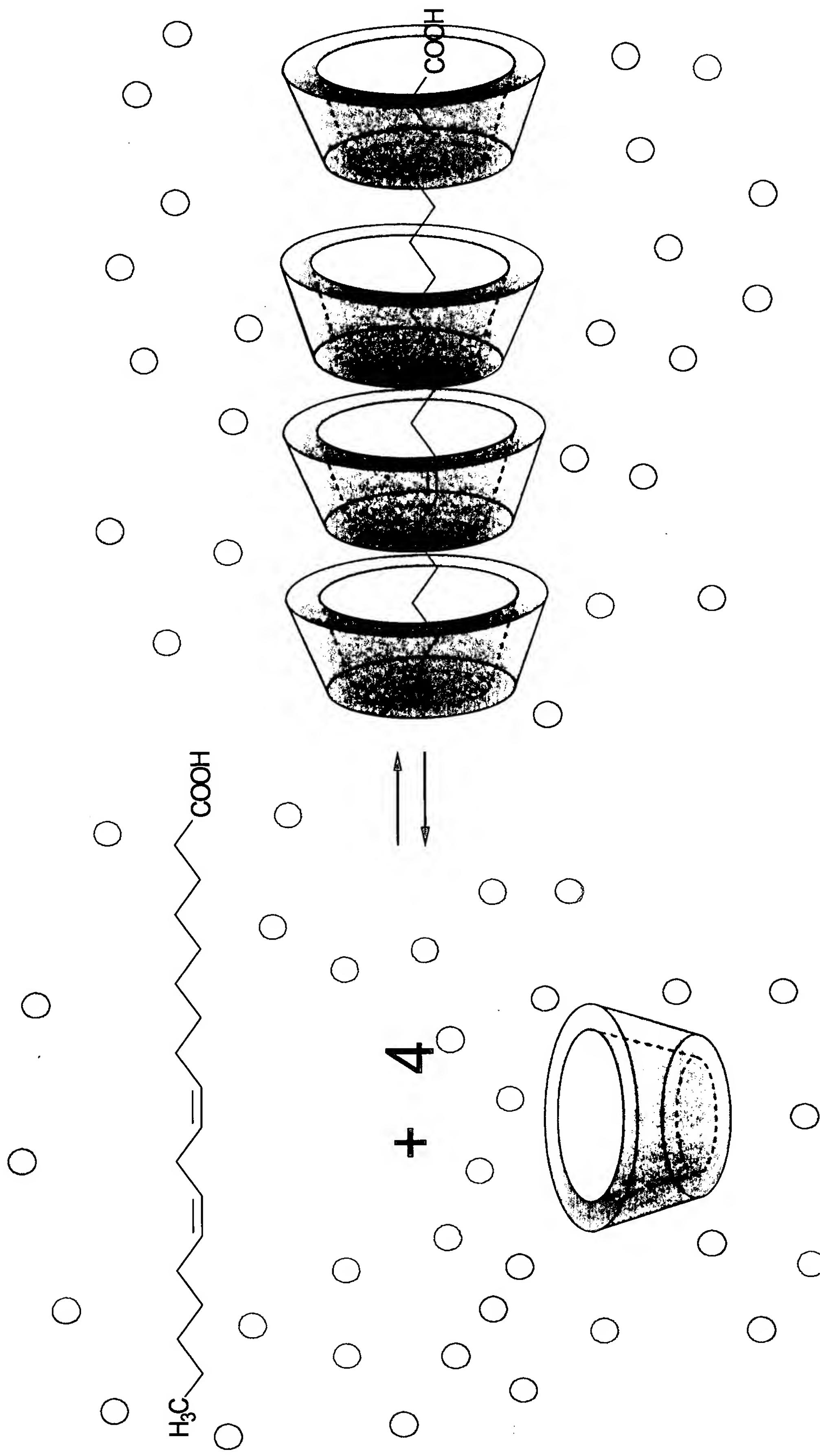
CAVAMAX®W6/LINOLEIC
ACID-COMPLEX



APPLICATION

- As component in cosmetic formulations like
 - emulsion, cream
 - gel
 - lip-balm
- Colour cosmetic, like lip-stick
 - face powder
 - eye shadow
 - face mask
- As component in derma products linoleic acid helps to cure
 - Skin disease
 - Sun burn
 - burns
 - akne vulgaris

Schematic representation of an inclusion complex formation between cyclodextrin and linoleic acid



CAVAMAX® W6/LINOLEIC ACID-COMPLEX, CHARACTERISTICS

CAVAMAX®W6-Complex

appearance:	white granulate/powder
active content:	min. 7.5 % (NMR, GC)
water content:	max. 14%
INCI names	cyclodextrin/linoleic acid
patent pending	DE 10253042.4-4; EP03026137.4; JP 2003-385675; KR 2003-0077579

BENEFITS OF CAVAMAX® W6/ LINOLEIC ACID -COMPLEXES BY APPLICATION IN FORMULATIONS

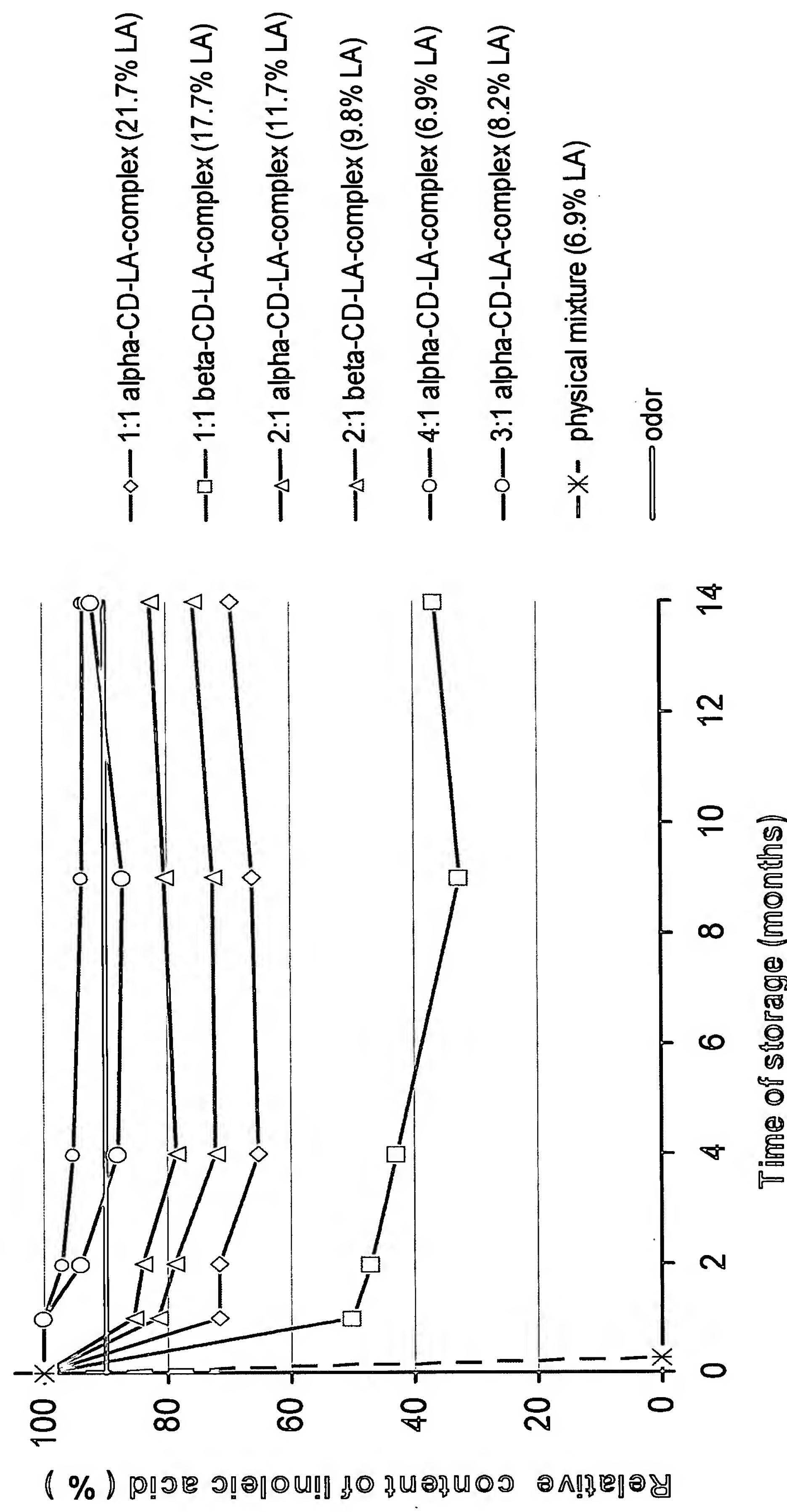
- Improved stability of linoleic acid e.g. oxygen, UV-A and UV-B and temperature
- Controlled release
- No rancidness in finished products e.g. during application
- No need of a stabiliser in cosmetic formulations
- Preparation of cosmetic formulations is even possible at higher temperatures
- Easy handling

BENEFITS OF CAVAMAX® W6/ LINOLEIC ACID-COMPLEXES BY APPLICATION IN FORMULATIONS

- Stable dispersion/emulsion
- Increase of texture of emulsions
- Efficient depot system
- Positive costs/benefit-factor
- Recommended dosage:
0.5 - 15% of CAVAMAX®W6/LINOLEIC ACID-COMPLEX
- In food products: improved taste and odor stability

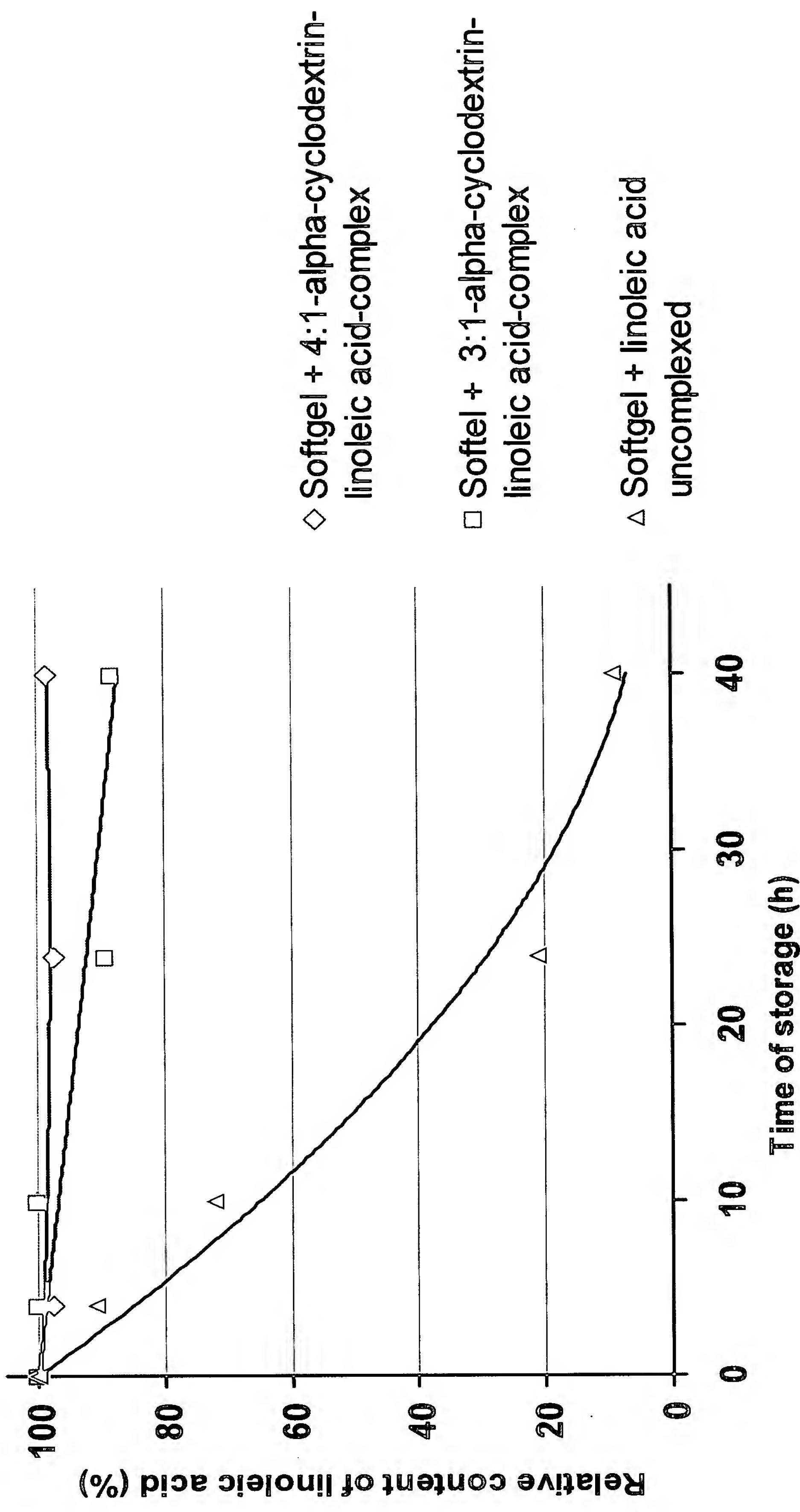
THERMOSTABILITY OF CAVAMAX®/LINOLEIC ACID-COMPLEXES WITH VARIOUS MOLAR RATIO OF ACTIVE AT 45°C

Stability at 45°C, stored in open vessels (90 mm diameter, 3 mm layer)



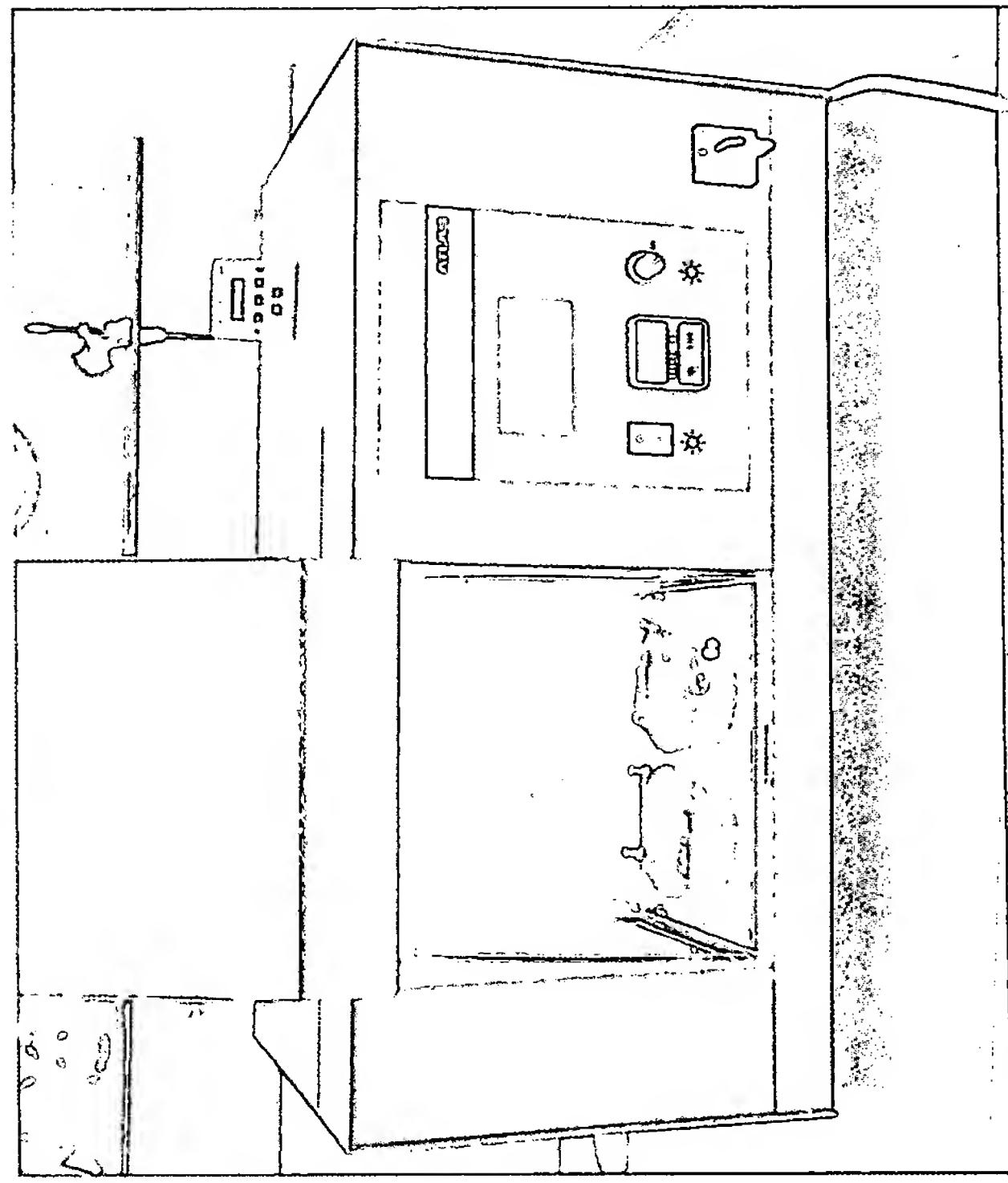
UV-STABILITY OF COMPLEXED AND UNCOMPLEXED LINOLEIC ACID IN GEL

Stability in Sun Screen Softgel (1.0 % linoleic acid. "Suntest" UV-A and UV-B, 45 °C)

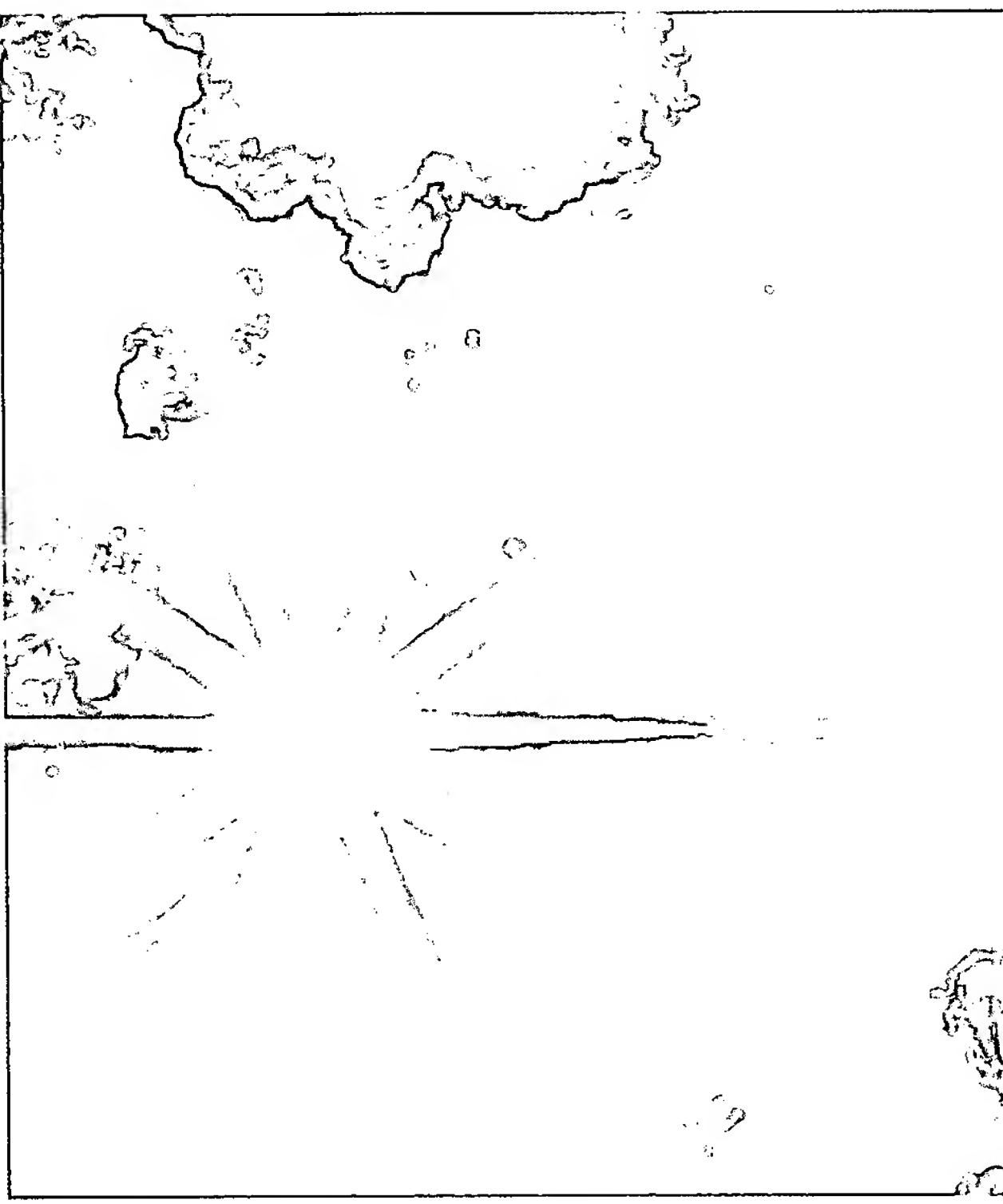


UV-STABILITY TEST IN SUN-TEST DEVICE: COMPARISON

SUN-Test device



“Sun-Bathing”



max. irradiation/day = 66 MJ/m²

irradiation/day (middle europe) = 5.7 MJ/m²

ratio (time lapse factor) =

11

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UV-A AND UV-B STABILITY TEST IN SUN-TEST EQUIPMENT

Method

- Equipment SUNTEST CPS from ATLAS
- Radiation-source Xenon-Lampe
- Optical filter Solar Standard
(filter referring to COLIPA* and DIN 67501)
max. determined inside-temperature = 45°C
- Air cooled sample room
- Maximum radiance $E (300\text{nm} - 800\text{nm}) = 765\text{W/m}^2$
- Constant controlling of the irradiation via photodiode

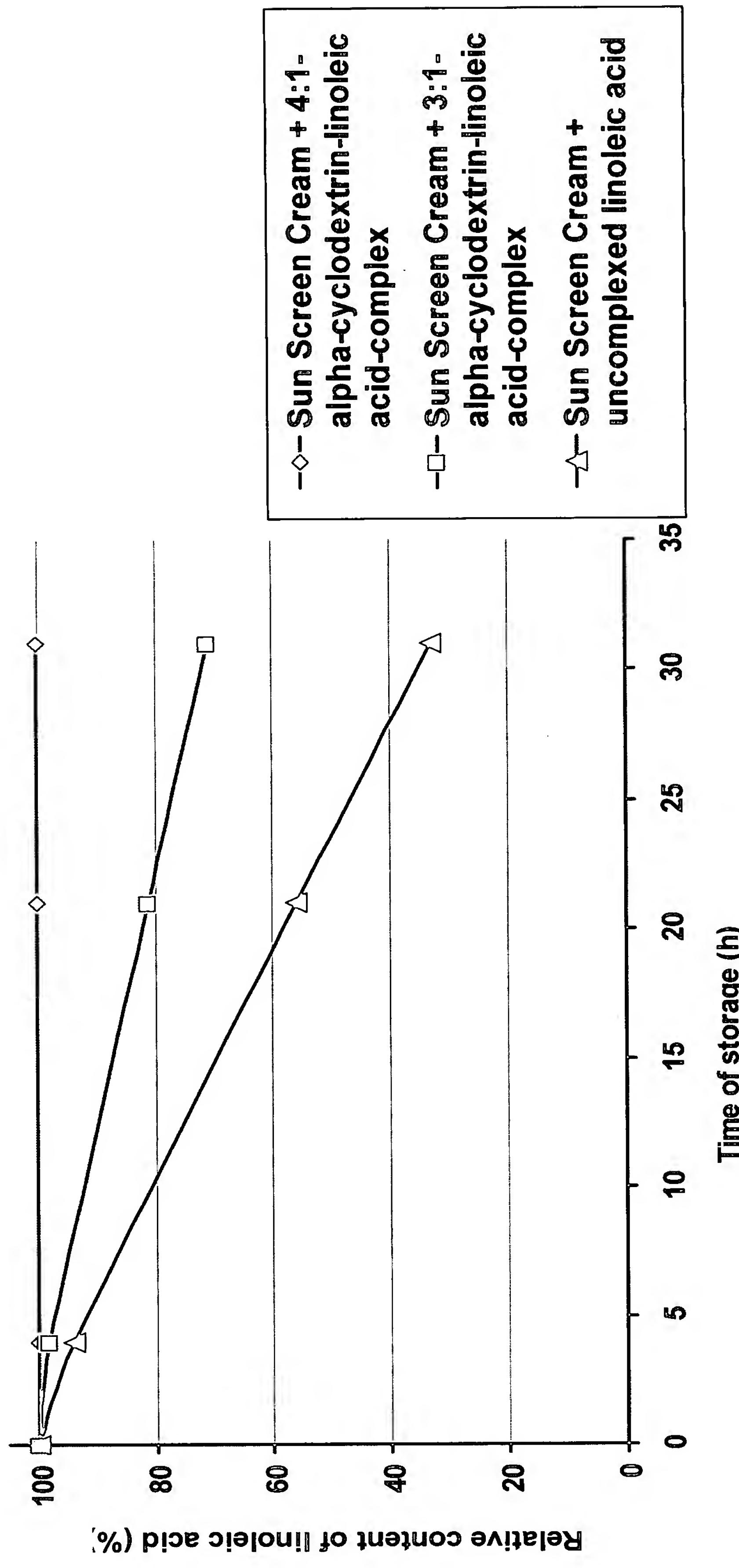
(source: ATLAS-Material Testing Solutions)

Sample preparation

- Solid substance like cyclodextrin-complex
3 – 4 g substance between 2 layers of glass 10 x 10 cm
(glass rim has to be covered with an adhesive tape)
- Soft substance like creams und pastes
3 – 4 g in a PE-plastic bag 10 x 10 cm (melted rim)

UV-STABILITY OF COMPLEXED AND UNCOMPLEXED LINOLEIC ACID IN CREAM

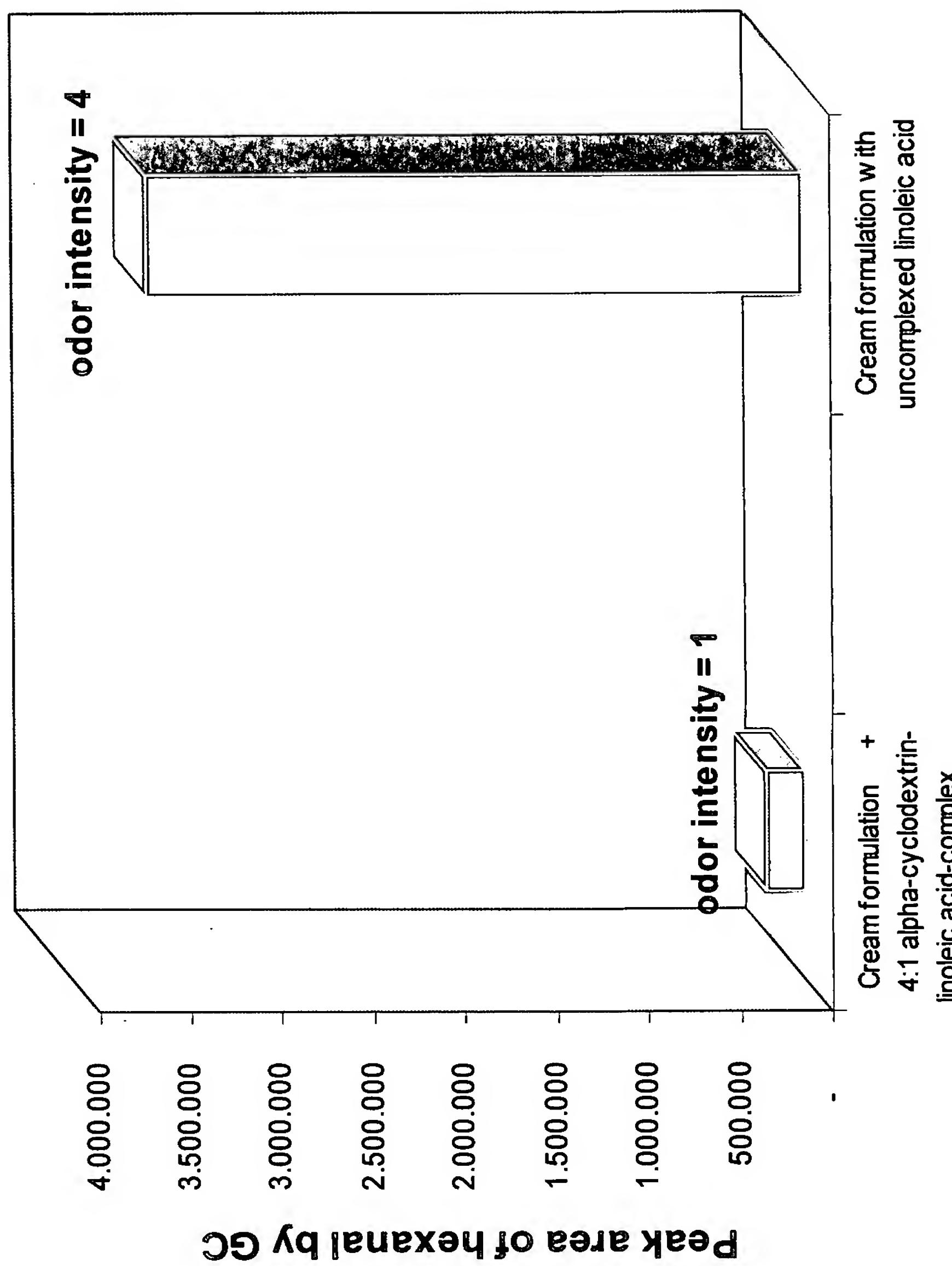
Stability in Sun Screen Cream (1.0 % linoleic acid content, "suntest" UV-A and UV-B, 45 °C)



LONG-TERM STABILITY OF 1% LINOLEIC ACID AS 4:1- ALPHA-CD/LA-COMPLEX AND UNCOMPLEXED IN CREAM

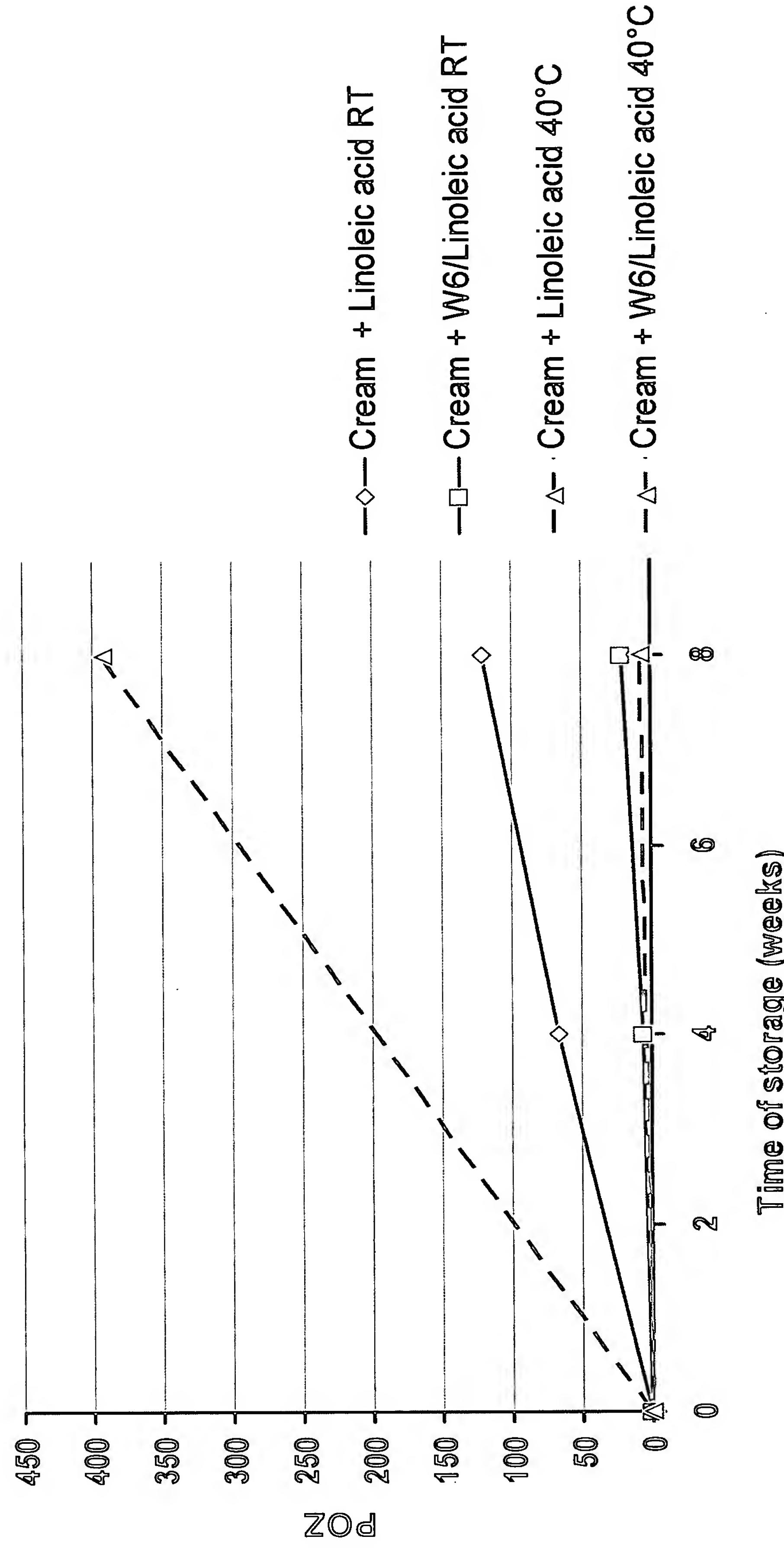
at room temperature after 12 months storage.

Sensory- and SPME/GC-Analysis of deteriorated linoleic acid e.g. as Hexanal



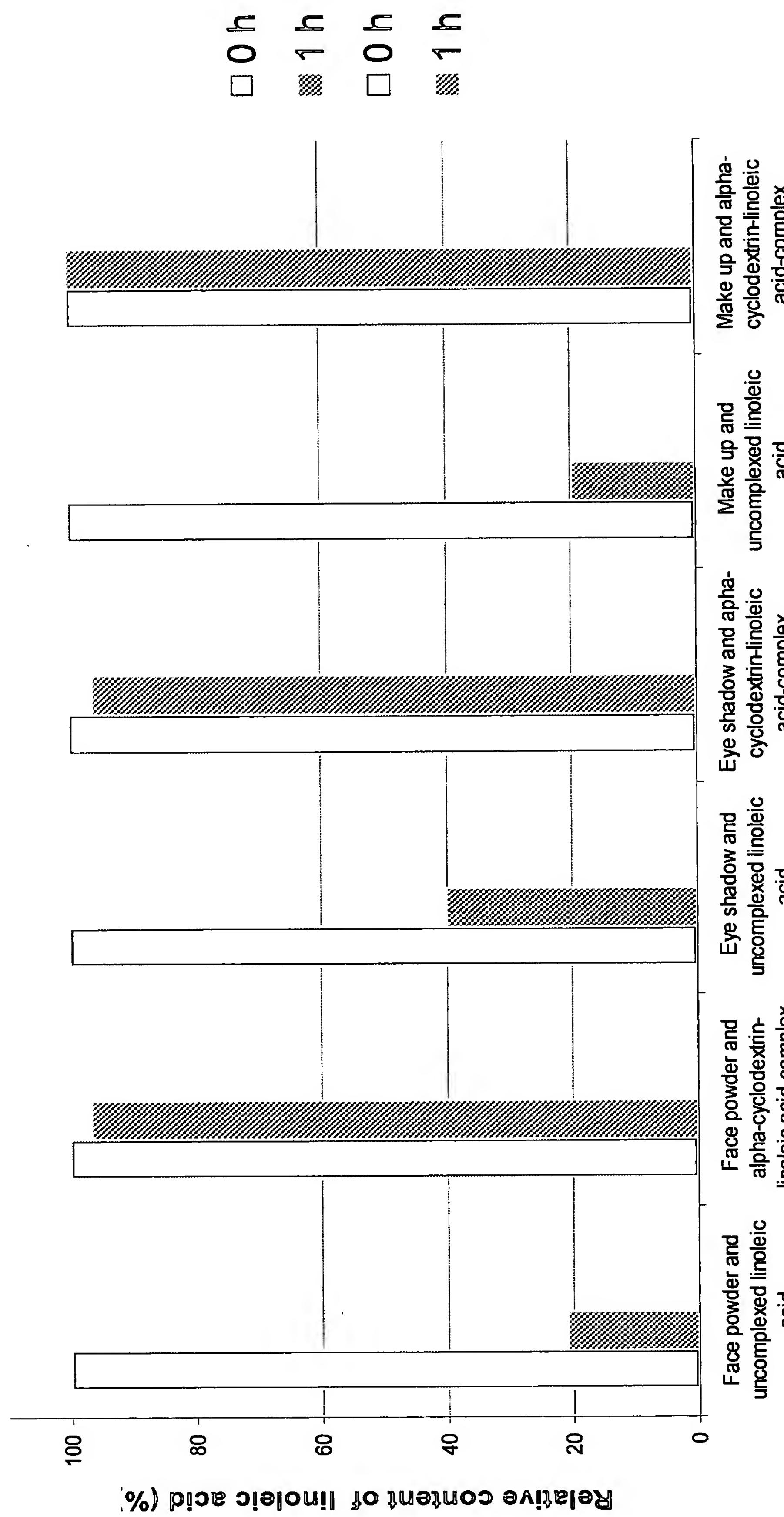
DEGRADATION OF COMPLEXED AND UNCOMPLEXED LINOLEIC ACID BY PEROXIDE VALUE

Instability in Cream W/O stored at different temperatures,
(1.0% linoleic acid content) determined by peroxide value



LIGHT-STABILITY OF 1% LINOLEIC ACID AS 4:1-ALPHA-CD/LA-COMPLEX AND UNCOMPLEXED IN COLOR-COSMETICS

“Sun-Test” UV-A and UV-B at 45 °C; GC-Analysis of Linoleic Acid-Content



DETERMINATION OF LINOLEIC ACID IN CYCLODEXTRIN AND COSMETIC PRODUCTS

Analytical Method

Principle of the Method:

Silylation by MSHFBA, GC-Direct Injection,

Internal Standard

Name of the analyte :

Retention times (min) :

Linoleic Acid

Analyte (Linoleic Acid)

Int.Std. (Eicosanoic Acid) 8,71

10,21 Cyclodextrin or Cosmetic Products

Solvent-Mix 80 % v/v Pyridine + 20 % v/v THF

Internal Standard ISTD

Eicosanoic Acid (C20) CAS - NR.: [530-30-9]

Internal Standard solution

Prepare a concentrated (e.g. about 1100 ppm) stock solution of Eicosanoic Acid in the solvent mix. Add a small volume (about 0.8 g) of that stock solution to (about 5g) of the Silylating Reagent MSHFBA to get a ISTD-working solution:
150 ppm ISTD in (MSHFBA > 95 %, < 5% solvent mix).

DETERMINATION OF LINOLEIC ACID IN CYCLODEXTRIN AND COSMETIC PRODUCTS

Sample preparation:

Dissolve the sample (Cyclodextrin 0.1 %, Cosmetic Products 1 %) in the solvent mix (rise in temperature, short ultrasonic agitation).

Silylating Reaction:

200 mg of the sample solution are diluted with 700 mg THF + 100 mg ISTD-working solution = 1000 mg reaction solution with 15 ppm ISTD. Heat the reaction mixture (70 °C, about 15 min) --- Alu Block Heater.

DETERMINATION OF LINOLEIC ACID IN CYCLODEXTRIN AND COSMETIC PRODUCTS

Calibration Range:

Analyte: 5 to 20 mg/kg solvent
ISTD: 15 mg/kg solvent

Calibration solutions:

Prepare solutions of linoleic acid and eicosanoic acid in the pyridine/THF-solvent mix separately and store them in a refrigerator (< 1 month, without silylation).

Dilute and mix the separate solutions to get ≥ 5 linoleic acid-calibration levels within the calibration range 5-20 ppm with constant 15 ppm ISTD-concentration for all levels.

Silylating Reaction:

Add 10 % (w / w) of the silylating reagent to the calibration solutions. Heat the calibration mixtures (70°C, about 15 min) --- Alu Block Heater.

Reagents:

THF p.A.
Pyridine
MSHFBA, N-Methyl-N-trimethylsilylheptafluorbutyramid (Macherey-Nagel)

DETERMINATION OF LINOLEIC ACID IN CYCLODEXTRIN AND COSMETIC PRODUCTS

GC - Operating Conditions

Instrument:	Gaschromatograph HP 6890 equipped with FID and autosampler				
Column:	30 m x 0.32 mm ID fused silica capillary column				
Stationary phase:	HP-5 Methyl-Polysiloxan with 5 % Phenyl-Polysiloxan				
Film Thickness:	df = 0,23 µm				
Supplier :	Agilent				
Column temperature:	Initial temp.	60 °C	Initial Time	1. 0 min	
Temp. program :	Program Rate A	30 °C / min	Program Rate B	- °C / min	
	Final Temp.	250 °C	Final Temp.	- °C	
	Final Hold Time:	7.0 min	Final Hold Time:	- min	
	Analysis Time:	min			
Carrier gas:	Helium				
Column Head Pressure:	117 kPa				
Flow Rate:	1,5 ml / min				
Electronic pressure control:	Constant Pressure				
Injection:	Direct Injection with autosampler HP 7673 A,				
	Splitless mode				

DETERMINATION OF LINOLEIC ACID IN CYCLODEXTRIN AND COSMETIC PRODUCTS

Inject samples:

Silylation reaction mixture of the calibration solutions and of the sample solution, respectively.

Injektionvolume (μL):

Inlet:

Temperature:
Split Flow:

Split/Splitless capillary inlet with EPC

300 °C
100 ml / min Purge B off 0 min
 Purge B on 0,9 min

Septum Purge :

Detector:

Hydrogen:

Air :

Make up gas:

Data acquisition and
quantitation software:

Appendix:

Representative GC-Run: Linoleic acid with Int. Standard Eicosanoic Acid after Silylation

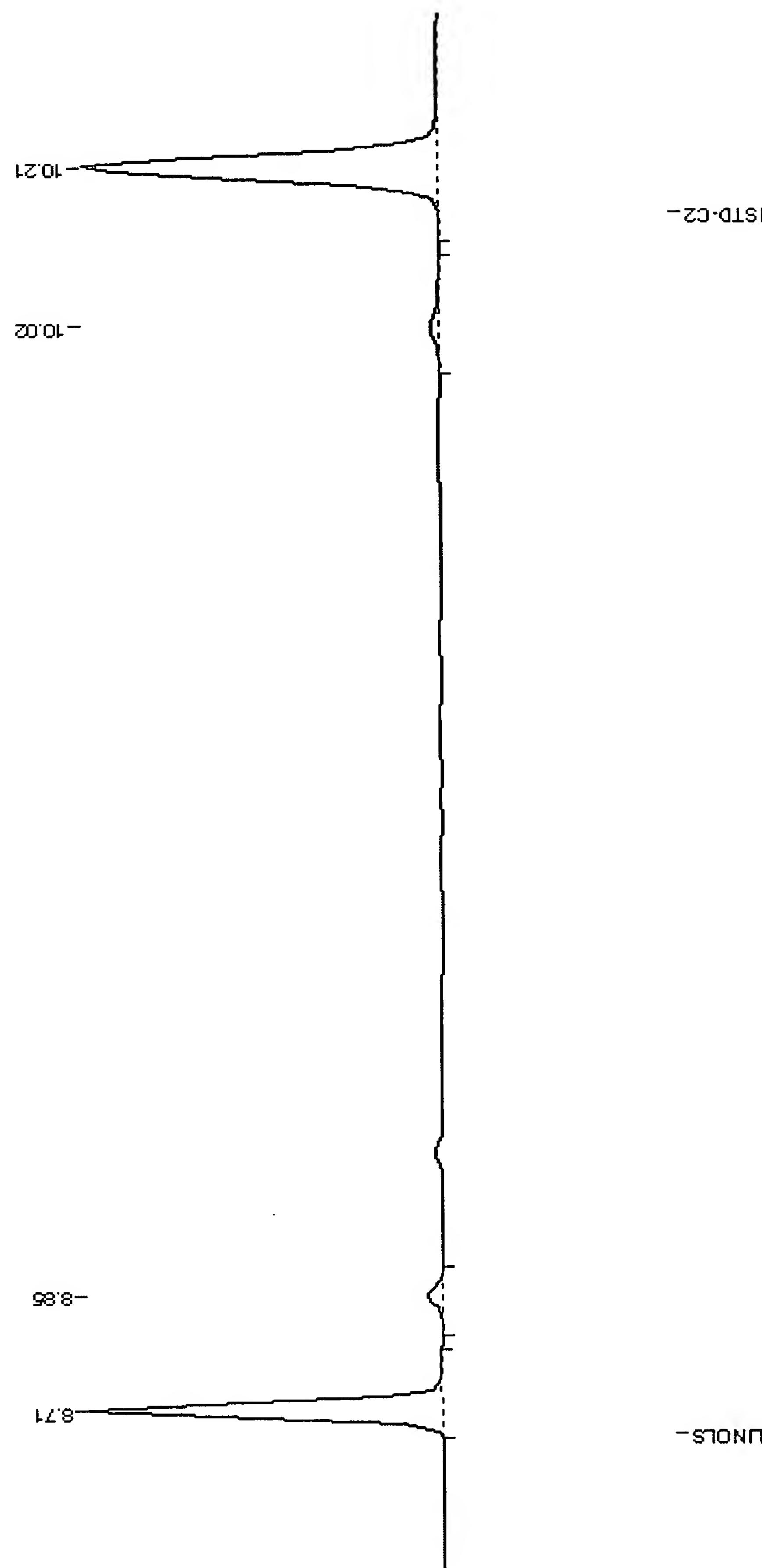
PE Turbochrome

Representative chromatogram

DETERMINATION OF LINOLEIC ACID IN CYCLODEXTRIN AND COSMETIC PRODUCTS

Representative GC-Run:

Linoleic Acid with Internal Standard Eicosanoic Acid after Silylation



WACKER

FINE CHEMICALS

CYCLODEXTRINS ANOTHER TOOL FOR ENCAPSULATION OF LINOLEIC ACID
Regert Mariës, F-I-P, February 2007, Slide 26

PREPARATION OF A SUN SCREEN SOFT STICK WITH (0.30 WW%) LINOLEIC ACID

	Ingredients	INCI-Names	w/w	Supplier
A) Vaseline	Petrolatum		68,9%	
	Stearoxy Dimethicone, Dimethicone		25,0%	Wacker-Chemie AG
B) CAVAMAX® W6/LINOLEIC ACID-COMPLEX (7.4% linoleic acid)	Cyclodextrin/Linoleic acid		4,0%	Wacker-Chemie AG
	Butyl Methoxydibenzoylmethane		2,0%	Givaudan
Parson 1789	Methylchloroisothiazolinone		0,1%	Rohm&Haas
	, Methylisothiazolinone			
Kathon CG			100,0%	

PREPARATION OF A SUN SCREEN SOFT STICK WITH (0.30 W/W%) LINOLEIC ACID

Calculation:

7.4g linoleic acid are related to 100g complex, 0.296g Linoleic acid related to x g complex

$$\frac{100\text{g} \times 0.296\text{g}}{7.4\text{g}} = 4.0\text{g}$$

Preparation:

Heat A to approx. 60°C and mix well, add B at approx. 45°C under stirring for about 15 minutes.

The content of linoleic acid in the formulation is detected by GC.

PREPARATION OF A SUN SCREEN SOFT GEL WITH (0.30 W/W%) LINOLEIC ACID

Ingredients	INCI-Names	w/w	Supplier
A) Water, dd	Aqua	86,8%	
CAVAMAX®W6/LINOLEIC ACID-COMPLEX (7.4% linoleic acid)	Cyclodextrin/linoleic acid	4,0%	Wacker-Chemie AG
Carbopol 940	Carbomer 940	2,5%	Noveon
Wacker Belsil® PDM 20	Phenyl Trimethicone	4,5%	Wacker-Chemie AG
Parsol MCX	Ethylhexyl Methoxycinnamate	2,0%	Givaudan
Kathon CG	Methylchloroisothiazolinone, Methylisothiazolinone	0,20%	Rohm&Haas
		100,0%	

PREPARATION OF A SUN SCREEN SOFT GEL WITH (0.30 W/W%) LINOLEIC ACID

Calculation:

7.4g linoleic acid are related to 100g complex, 0.296g Linoleic acid related to x g complex

$$\frac{100\text{g} \times 0.296\text{g}}{7.4\text{g}} = 4.0\text{g}$$

Preparation:

Mix all ingredients at approx. 40°C.

The content of linoleic acid in the formulation is detected by GC.

PREPARATION OF A SUN SCREEN CREAM WITH (0.30 WW%) LINOLEIC ACID

Ingredients	INCI-Names	w/w	Supplier
A) Water, dd	Aqua	60,7%	
CAVAMAX®W6/LINOLEIC ACID-COMPLEX (7.4% linoleic acid)	Cyclodextrin/linoleic acid	4,0%	Wacker-Chemie AG
Carbopol 934 Polymer (1% solution)	Carbomer	5,0%	Noveon
Tetrasodium EDTA	Tetrasodium EDTA	0,20%	
Glycerine	Glycerine	2,5%	
Triethanolamine	Triethanolamine	1,0%	
B) Wacker Belsil® DM 350	Dimethicone	2,0%	Wacker-Chemie AG
Isopropyl Myristate	Isopropyl Myristate	9,0%	
Stearyl Alkohol	Stearyl Alkohol	9,5%	
Cetyl Alkohol	Cetyl Alkohol	0,50%	
Stearic Acid	Stearic Acid	3,0%	
Sodium Stearat	Sodium Stearat	1,0%	
Parsol MCX	Ethylhexyl methoxycinnamate	1,5%	Givaudan
C) Kathon CG	Methylchloroisothiazolinone, Methylisothiazolinone	0,10%	Rohm&Haas
		100,0%	

PREPARATION OF A SUN SCREEN CREAM WITH (0.30 WW%) LINOLEIC ACID

Calculation:

7.4g linoleic acid are related to 100g complex, 0.296 g linoleic acid related to x g complex

$$\frac{100\text{ g} \times 0.296\text{ g}}{7.4\text{ g}} = 4.0\text{ g}$$

Preparation:

- mix the components of phase A) at 70°C
- mix the components of phase B) at 70°C
- than pour phase A) in phase B) under intense stirring
- after cool down to 45°C add finally phase C)

The content of linoleic acid in the formulation is detected by GC as described

PREPARATION OF A BELSIL FOUNDATION WITH (0.30 WW%) LINOLEIC ACID

Ingredients	INCI-Names	w/w	Supplier
A) Wacker Belsil® DM 1 plus	Dimethicone	10,00%	Wacker-Chemie AG
Wacker Belsil® CM 7026 VP	C26-28 Alkyl Methicone	2,70%	Wacker-Chemie AG
Wacker Belsil® SPG 128 VP	Cyclopentasiloxane and Caprylyl Dimethicone Ethoxy Glucoside	11,0%	Wacker-Chemie AG
Wacker Belsil® DM 5	Cyclomethicone	2,30%	Wacker-Chemie AG
Hostacerin DGI	Polyglyceryl-2 Sesquiosostearate	2,40%	Clariant
Wacker Belsil® TMS 803	Trimethylsiloxysilicate	1,50%	Wacker-Chemie AG
B) Mixture of ferric oxide and titanium dioxide		8,50%	
Talc	Talc	5,00%	Grolman
C) Water, dd	Aqua	50,2%	
Sodium chloride	Sodium Chloride	2,00%	Merck
CAVAMAX®W6/LINOLEIC ACID-COMPLEX (7.4% linoleic acid)	Cyclodextrin / linoleic acid	4,00%	Wacker-Chemie AG
D) Fragrance	Perfume	0,30%	
Kathon CG	Methylchloroisothiazolinone, Methylisothiazolinone	0,10%	Rohm&Haas
		100,0%	

PREPARATION OF A BELSIL FOUNDATION WITH (0.30 WW%) LINOLEIC ACID

Calculation:

7.4g linoleic acid are related to 100g complex, 0.296 g linoleic acid related to x g complex

$$\frac{100\text{ g} \times 0.296 \text{ g}}{7.4 \text{ g}} = 4.0 \text{ g}$$

Preparation:

- mix the components of phase A) at 75°C
- mix the components of phase B) and add to A) under intense stirring
- disperse the complex in phase C) at 50°C
- than pour slowly phase C) to the mixture of phase A) and B)
- after cool down to 45°C add finally phase D)
- than stir till the mixture is homogenous

The content of linoleic acid in the formulation is detected by GC

SUPPLEMENTS

- Page 27, 28, 29, 30, 31, 32 ,33 and 34 on 15.03 2006, adapted formulation recipe
- Page Wacker AG 27, 29, 31 ,33 on 10.08.2006, adapted formulation recipe
- Page 18 revised
- Page 33 and 34 revised

CAVAMAX®W6/LINOLEIC ACID - COMPLEX

**Consumer expect just high-quality skincare products with
extraordinary performance**